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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,845	08/01/2003	Stephen Richmond	078883-0166	1041

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EXAMINER	
BOWERS, NATHAN ANDREW	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/631,845	RICHMOND ET AL.	
	Examiner	Art Unit	
	Nathan A. Bowers	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *033006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 10 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uber "Application of robotics and image processing to automated colony picking and arraying" in view of Bienert (US 20010019845).

Uber discloses in the *Introduction* an apparatus for picking cell colonies comprising an apparatus bed for arranging a sample container comprising a plurality of cell colonies. The *Imaging System* and *Imaging Procedure* sections disclose a camera and image processing software useful in identifying animal cell colony locations from captured images. A picking head movable around the apparatus bed using positioning motors to cell colony locations identified by the image processing software is additionally provided with a transfer pipette. See the *Robotic System* section. The distal end of the pipette is introduced by a drive into a sample container offset from a cell colony. Since pipettes capable of moving fluids and cells through suction are disclosed, the invention must inherently include a pressure controller that is operable to aspirate quantities of the medium. The apparatus inherently could be used for picking animal cell colonies held in a medium since an automated picker, a camera, imaging processing software, and dispensing containers are all incorporated into the system design. Uber, however, does not expressly disclose a plurality of hollow pins connected to the picking head.

Bienert discloses an automatically controlled metering head comprising a plurality of micropipette tubes (Figure 2:250) capable of aspirating fluids from a sample container and disposing of the fluids in a dispensing container. This is disclosed in paragraphs [0012]-[0027].

Uber and Bienert are analogous art because they are from the same field of endeavor regarding the automatic transfer of samples using a picking head with at least one hollow pin.

At the time of the invention, it would have been obvious to construct the apparatus disclosed by Uber with a picking head comprising a plurality of hollow pins capable of independently collecting cell samples using suction, and subsequently dispensing the samples at a different location. Bienert teaches in paragraph [0011] that picking heads comprising multiple hollow pins can more efficiently transfer a large number of samples since a plurality of samples may be transported at one time. The simultaneous processing of a plurality of samples in parallel is advantageous because the sampling process can be accomplished more quickly with better accuracy.

2) Claims 1, 3, 10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) in view of Elverd (GB 2310006).

Magnuson discloses a method and apparatus for the automated picking of animal cell colonies. This is disclosed in paragraph [0015]. Paragraphs [0068], [0119]-[0130], and [0178] teach that a picking head comprising a hollow pin (Figure 3) is moveable about the apparatus using positioning motors. A dispensing container and a sample container including a plurality of animal cell colonies held in a medium are placed onto the apparatus according to paragraphs [0117] and [0132]. Magnuson discloses in paragraphs [0015] and [0059] that the dispensing

container comprises an array of wells separated by a characteristic spacing. Paragraph [0068] states that machine vision and image processing features are used to identify animal cell colony locations in the sample container, and the picking head is moved to above the sample container in response. Specifically, paragraphs [0018] and [0074] disclose a camera as a useful image capturing device, and paragraphs [0099]-[0102] disclose image processing software. Paragraph [0069] and [0117] teach that the hollow pin is aligned with the animal cell colony locations, and that a distal end of the hollow pin is introduced into the cell medium proximate to the animal cell colony by an offset distance. Cells are aspirated into the hollow pin and expelled into the dispensing container through the movement of the picking head. Magnuson, however, does not expressly disclose a plurality of hollow pins used in the collection of animal cells.

Elverd discloses a picking head comprising a plurality of pins capable of automatically transporting biological cells from a sample container to a dispensing container. This is taught on page 2. Pins are selectively moved into a transfer position and simultaneously or independently activated in order to collect samples in parallel. It is apparent from Figure 1 that Elverd's invention is capable of aligning with the characteristic spacing of a well plate array.

Magnuson and Elverd are analogous art because they are from the same field of endeavor regarding the automatic collection and dispersion of biological samples.

At the time of the invention, it would have been obvious to ensure that the invention disclosed by Magnuson contained a plurality of hollow pins each individually aligned with the characteristic spacing of the wells located in the dispensing container. Elvert teaches on page 1 that the simultaneous processing of a plurality of samples in parallel is advantageous because the sampling process can be accomplished more quickly with better accuracy. The use of multiple

hollow tubes correlating to multiple wells reduces cross contamination since different tubes are used to collect different samples. The process can be easily automated to enhance reproducibility.

With respect to claim 2, Magnuson and Elvert disclose the method in claim 1. Magnuson additionally teaches that the picking step comprises repeating the aligning and aspirating steps for multiple ones of the hollow pins to pick multiple ones of the animal cell colonies. This is taught in paragraph [0059].

With respect to claims 5 and 6, Magnuson and Elvert disclose the method in claim 1. In addition, Magnuson teaches that the animal cell colonies are stained either with a contrast enhancing agent or a fluorescent agent to assist the imaging processing. In paragraph [0111], Magnuson teaches that dark field microscopy and fluorescence-assisted detection can be employed in the invention.

With respect to claims 18, 19, 21, and 22, Magnuson and Elvert disclose the method and apparatus in claims 1 and 10. In addition, Magnuson teaches that the animal cell colony comprises either a plurality of cells or a single cell. Paragraphs [0116]-[0118] teach that the invention may be used to process a plurality of cells or a single cell.

3) Claim 4, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) in view of Elverd (GB 2310006) as applied to claims 1 and 10, and further in view of Sogi (US 4210724).

Magnuson and Elvert disclose the method and apparatus set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step. Magnuson does not disclose a drive mechanism for causing lateral or rotary motion of the distal ends of the pins to facilitate detachment of animal cell colonies.

Sogi discloses an apparatus for automatically transporting cells in a culturing solution to a dispensing container by collecting the desired cells in a pipette through suction. This is taught in the abstract and in column 10, line 54 to column 11, line 48. Column 11, line 49 to column 13, line 16 teach that a drive mechanism is provided to cause the tip of the pipette to quickly oscillate in the culture solution during collection in order to facilitate detachment of cell colonies adhered to the sample container. The pipette is intrinsically capable of performing both lateral and rotary oscillations.

Magnuson, Elvert, and Sogi are analogous art because they are from the same field of endeavor regarding the automatic collection and transportation of cultured cells.

At the time of the invention, it would have been obvious to provide Magnuson and Elvert's invention with a drive mechanism capable of oscillating the distal ends of the pins in

order to facilitate, during collection, the detachment of animal cell colonies adhered to the sample container. Sogi teaches in column 3, lines 36-40 and column 13, lines 33-42 that automatic agitation of the culture solution is a highly efficient way to ensure that the cells are suspended in the sample and fully gather during the collection process. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells by producing turbulence in the medium.

4) Claims 4, 7-9, 14-17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magnuson (US 20030179916) in view of Elverd (GB 2310006) as applied to claims 1 and 10, and further in view of Parekh (US 6064754).

With respect to claim 4, Magnuson and Elvert disclose the method set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Magnuson discloses in paragraphs [0011] and [0020] that the animal cell colonies are adhered to the sample container and immersed in a medium. Magnuson, however, does not expressly disclose that the distal end of the pin is agitated relative to the sample container so as to produce turbulence in the medium to detach the animal cell colony at the location prior to performing the aspirating step.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55

indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 13, line 56 to column 14, line 7 teaches that the tips of the picking apparatus are agitated relative to the sample container in order to collect the target material. This agitation intrinsically must produce turbulence in the medium.

Magnuson, Elvert, and Parekh are analogous art because they are from the same field of endeavor regarding the automatic imaging, collection, and dispensing of biological components.

At the time of the invention, it would have been obvious to agitate the distal ends of the pins located in the picking apparatus disclosed by Magnuson and Elvert. Magnuson teaches in paragraph [0011] that animal cells are characterized by a high affinity for the surfaces upon which they are immobilized during growth. In this way, agitation and scraping forces would have been necessary to dislodge the adherent cells from their growth substrates. Therefore, it would have been obvious to use the distal ends of the tips to dislodge the target cells through direct contact or by producing turbulence in the medium.

With respect to claims 7-9 and 14-16, Magnuson and Elvert disclose the method and apparatus set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the plurality of animal cell colonies comprise or express a biological molecule of interest, namely biopharmaceutical proteins.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 2, lines 8-20 and column 4, lines 20-51 teach that the biological material may comprise biopharmaceutical proteins expressed from a cell

culture. Column 7, lines 13-20 state that the proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55 indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis.

At the time of the invention, it would have been obvious to use Magnuson and Elvert's invention to selectively aspirate and dispense animal cells that express biological molecules, and, more specifically, biopharmaceutical proteins. In column 2, lines 8-20, Parekh teaches that the presence, absence, or altered expression of many different proteins can be associated with a disease or a condition of interest. Studying the expression of these products using Magnuson and Elvert's device would therefore been advantageous in order to better understand physiological problems associated with difficulties in gene expression. Furthermore, biomolecules are often useful as therapeutic agents, and as markers for diagnosis, prognosis, and evaluating response to treatment. Therefore, it would have been beneficial to develop methods designed to detect, isolate, and consolidate animal cells that express biopharmaceutical proteins in order to produce a cell product that has valuable medicinal or therapeutic applications.

With respect to claims 17 and 20, Magnuson and Elvert disclose the method and apparatus set forth in claims 1 and 10 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the animal cell colonies are held suspended in the medium.

Parekh discloses a computer assisted isolation system for removing biological material from selected spots on a biological plate. Column 7, lines 13-20 state that proteins are fluorescently labeled and detected by an image processing means, and column 13, lines 15-55

indicate that an automated picking apparatus is provided for collecting a desired protein through suction and moving the sample to a separate dispensing container for analysis. Column 2, lines 21-49 teach that the target biological materials are suspended in a semi-solid gel prior to collection by the picking apparatus.

At the time of the invention, it would have been obvious to suspend the animal cells disclosed by Magnuson in a semi-solid gel rather than allowing the cells to adhere to the sample container. In column 6, lines 2-12, Parekh teaches that gels are capable of suspending biological materials prior to collection, and are non-interfering with respect to fluorescence detection and image processing. Applicant teaches on page 1 of the specification that mammalian cell colonies held in suspension in a semi-solid medium are well known in the art.

Response to Arguments

Applicant's arguments filed 04 April 2006 have been fully considered but they are not persuasive.

With respect to the 35 U.S.C. 103 rejections involving Magnuson in view of Elverd, Applicant's principle arguments are

(a) Magnuson's method of picking involves contacting the picking pin to the base of the sample container, and therefore causes damage to the picking pin and the animal cell colony. The present inventors, however, discovered that an animal cell colony may be removed by aspiration alone, and that contact between the picking pin and the sample container is unnecessary. Magnuson does not teach that there are problems with contact picking, so it provides no motivation for adopting non-contact picking teachings.

In response to Applicant's arguments, please consider the following comments.

Magnuson discloses an apparatus for picking animal cell colonies. Paragraphs [0020], [0024] and [0124] indicate that a picking tip is implemented that is capable of removing cell colonies from a surface using aspiration alone. Magnuson teaches that scraping can be used, but is entirely optional. It is agreed that Magnuson states that the tip contacts the cells during collection, however it is believed that this contacting does not damage the cells since only aspiration (not scraping) is implemented.

Regardless, there are no limitations in the claims that state that the picking pin cannot contact the cell colonies or the cell colony holders. Therefore, arguments regarding whether or not Magnuson teaches that it is necessary to contact the picking pin to the sample container are not relevant to the prosecution of the claims.

With respect to the 35 U.S.C. 103 rejections involving Uber in view of Bienert, Applicant's principle arguments are

(a) Uber does not disclose the integration of an imaging system and picking robot. Rather, it explicitly states, "We have not attempted to physically integrate the two units ..."

In response to Applicant's arguments, please consider the following comments.

Uber discloses an imaging unit and a picking robot that are separate parts of the same system. The imaging unit and the picking robot represent individual components that make up the overall animal cell picking apparatus. They are in communication with each other since the picking robot responds to information obtained from the imaging unit. This arrangement meets every limitation set forth in claims 10 and 21. For the sake of argument, even if the claims did

require physical integration of the imager and picking head, Uber suggests on page 642, column 3 that it is possible and desirable to physically combine the two units. "Since the imaging process requires several manual steps for each petri dish, we image a batch of dishes entirely by hand...Imaging and picking could be physically integrated if the manual steps were automated."

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NAB

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